P29690.A06

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Ghita LANZENDORFER et al.

Confirmation No. 3976
Group Art Unit: 1617

Serial No. : 08/849,525

Examiner: Cotton, Abigail Manda

Filed : August 29, 1997

For : USE OF FLAVONOIDS AS IMMUNOMODULATING OR IMMUNO-PROTECTIVE AGENTS IN COSMETIC AND DERMATOLOGICAL PREPARATIONS

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window, Mail Stop AF
Randolph Building
401 Dulany Street
Alexandria, VA 22314

Sir:

Applicants hereby request review of the final rejection of claims 37-56 dated September 13, 2006 in the above-identified application. No amendments are being filed with the request.

This request is being filed with a notice of appeal.

The review is requested for the reasons stated on the attached five sheets.

If there are any questions about this application, the Examiner is invited to contact the undersigned at the telephone number listed below.

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Respectfully submitted,
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ANNEX TO THE APPEAL BRIEF REQUEST FOR REVIEW OF REJECTION OF CLAIMS 37-56 OF APPLICATION NO. 08/849,525

The following is Appellants' statement pointing out clear errors in the Examiner's rejection and the Examiner's omissions of essential elements needed for a *prima facie* rejection:

Claims 37, 38, 43 and 48-50, including both of the present independent claims 37 and 55, are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Evans et al., U.S. Patent No. 5,358,752 (hereafter "EVANS") in view of Suzuki et al. U.S. Patent No. 5,145,781 (hereafter "SUZUKI"), and as evidenced by the entry in *Harrison's Principles of Internal Medicine*, 1994, New York, McGraw-Hill, Inc., 13th ed., pp. 309-313 (hereafter "HARRISON").

The rejection essentially alleges that EVANS teaches the topical application to skin of a composition comprising an antioxidant to control the oxidative damage of skin caused by UV radiation, that SUZUKI teaches that alpha-glycosyl rutin (which comprises alpha-glucosyl rutin) has properties as an antioxidant and is a UV absorbent and can be provided in pharmaceuticals and cosmetics, and that HARRISON teaches that excessive exposure to UVB radiation is implicated in the development of a number of skin disorders, including the immunosuppression of skin cells, wherefore the combined teachings of EVANS, SUZUKI and HARRISON allegedly render it obvious to one of ordinary skill in the art to use a flavonoid such as alpha-glucosyl rutin for the treatment or modulation of immunosuppression of skin cells induced by UVB radiation as recited in present independent claim 37.

Applicants respectfully disagree with the Examiner in this regard. In particular, there is no motivation to combine the teachings of EVANS and SUZUKI, let alone to combine these documents with HARRISON.

Applicants note that the rejection relies particularly on the abstract of EVANS according to which the phenolic diterpene compound of the ferruginol type disclosed therein (carnosic acid) can be incorporated in skin care products to reduce the accumulation of lipid peroxides and other biological oxidation products in the skin that result from sunlight, heat and radiation. SUZUKI mentions that alpha-glycosyl rutin, when used in pharmaceuticals, "acts as antioxidant to exhibit activities of removing activated oxygen and suppressing the formation of lipoperoxides" and that this "is convenient in the prevention and treatment of susceptive diseases and also in the maintenance and promotion of health." Col. 8, lines 19-25 of SUZUKI.

The only "link" between EVANS and SUZUKI identified by the Examiner appears to be the mentioning of the reduction of the accumulation of lipid peroxides by a phenolic diterpene compound of the ferruginol type in EVANS and the mentioning of the suppression of the formation of lipoperoxides by alpha-glycosyl rutin in SUZUKI. This "link" would allegedly motivate one of ordinary skill in the art to use alpha-glycosyl rutin (and specifically, alpha-glucosyl rutin) in the cosmetic compositions of EVANS (presumably in addition to or instead of the phenolic diterpene compound of the ferruginol type).

It is not seen that EVANS provides motivation to replace or supplement the phenolic diterpene compound of the ferruginol type specifically taught therein by any other antioxidant, let alone by a flavonoid such as alpha-glucosyl rutin. In this regard, it

is pointed out that EVANS mentions that the use of antioxidants to inhibit peroxidation is well known and that a number of antioxidants have been used in cosmetic compositions, examples thereof being ascorbic/erythorbic acids and related compounds, tocopherols, BHA, BHT and hydroquinone. Col. 1, lines 30-37. Despite the existence of these well known and conventional antioxidants, EVANS does not recommend the use thereof but teaches the use of specific antioxidants, i.e., carnosic acid and related compounds.

SUZUKI fails to teach or suggest that alpha-glycosyl rutin (alpha-glucosyl rutin) would be a better antioxidant than any of the conventional antioxidants whose use in cosmetic compositions is acknowledged by EVANS but not recommended for use in the compositions disclosed therein.

In particular, while SUZUKI mentions that alpha-glycosyl rutin (alpha-glucosyl rutin) "acts as antioxidant to exhibit activities of removing activated oxygen and suppressing the formation of lipoperoxides", this would appear to be a property which alpha-glycosyl rutin (alpha-glucosyl rutin) shares with many, if not all, antioxidants, including the conventional antioxidants specifically mentioned by EVANS.

Further, the activity of alpha-glycosyl rutin (alpha-glucosyl rutin) with respect to the removal of activated oxygen and the suppression of the formation of lipoperoxides is mentioned in SUZUKI only in the context of pharmaceutical compositions, not in the context of cosmetic compositions. For instance, only Examples B-10 and B-11 of SUZUKI (which describe pharmaceutical compositions for injection) mention the removal of activated oxygen and the suppression of the formation of lipoperoxides by

alpha-glycosyl rutin whereas the Examples of SUZUKI which describe cosmetic compositions, i.e., Examples B-9, (B-13), B-14 and B-15, are silent in this regard.

Even further, even if one were to assume, *arguendo*, that one of ordinary skill in the art would be motivated to replace or supplement the phenolic diterpene compound of the ferruginol type used in the compositions of EVANS by alpha-glucosyl rutin, it is not seen that in this case HARRISON would render it obvious to employ a corresponding composition for the treatment or modulation of immunosuppression of skin cells induced by UV radiation. It is noted that in this regard the rejection alleges that HARRISON teaches that excessive exposure to UVB radiation is implicated in the development of a number of skin disorders, including the immunosuppression of skin cells.

Applicants are unable to see how HARRISON can render it obvious to one of ordinary skill in the art to use a composition which comprises alpha-glucosyl rutin for the treatment or modulation of immunosuppression of skin cells induced by UVB radiation.

In this regard, it is pointed out that HARRISON fails to link immunosuppression and the formation of lipoperoxides or any other oxidation products. In fact, HARRISON is completely silent in this regard and the explanation for UVB induced immunosuppression offered by HARRISON has nothing to do at all with oxidation, let alone with the formation of lipoperoxides.

Specifically, according to the last paragraph in the right column of page 309 of HARRISON, "UV-B appears to be the most efficient in altering immune responses, likely related to the capacity of such energy to affect antigen presentation in skin by interacting with epidermal Langerhans cells." HARRISON further explains that

"[f]ollowing skin exposure to erythema doses of UV-B, Langerhans cells undergo both morphologic and functional changes that result in decreased contact allergic responses when haptens are applied to the radiated site. This diminished capacity for sensitization is due to the induction of antigen-specific suppressor T lymphocytes. Indeed, while the immunosuppressive effect of irradiation is limited to haptens applied to the irradiated site, the net result is systemic immune suppression to that antigen because the induction of suppressor T cells that spread throughout the body."

The above passages of HARRISON make it more than apparent that even in light of the disclosures of EVANS and SUZUKI there is no reason whatsoever to expect that by applying a cosmetic composition which comprises a flavonoid such as alpha-glycosyl rutin the immunosuppression induced by UVB radiation can be treated or modulated. The Examiner has not provided any evidence at all which would make it reasonable to expect that by reducing or inhibiting the formation of lipoperoxides taught by EVANS and SUZUKI morphological and functional changes in Langerhans cells and thus, immunosuppression can be inhibited. In other words, there is no expectation of success.

HARRISON does not provide any evidence whatsoever that someone who has been "excessively" exposed to UVB radiation would apply the composition of EVANS (with or without alpha-glucosyl rutin) and thereby (necessarily) treat or modulate the immunosuppression of skin cells induced by UV radiation.

To sum up, for at least all of the foregoing reasons, the Examiner has failed to establish a *prima facie* case of obviousness with respect to any of the rejected claims.